ANTI -ASTHMATIC DRUGS

Asthma is most common respiratory tract infection. It is the reversible obstruction of large and small airways. Bronchial asthma is characterized by hyperresponsiveness of tracheo-bronchial smooth muscle to a variety of stimuli, resulting in narrowing of air tubes, often accompanied by increased secretions, mucosal edema and mucus plugging.

1. Inflammation
2. Hyper reactivity
3. Bronchosp

asm **Types of**

Bronchial

Asthma

1. Extrinsic Asthma: (allergic) It is mostly episodic, less prone to status asthmaticus

Atopic (immediate due to IgE antibody).

Nonatopic delayed for some hours, associated with production of precipitatingantibodies

2. Intrinsic Asthma

It tends to be perennial, status asthmaticus is more common. Associated with COPD.

Classification

Sympathomimetics :*Short Acting:* ***Salbutamol,***

Terbutaline*Long Acting:* ***Formeterol, Salmetrol,***

Bambuterol **Mechanism of Action**

1. Beta-2 adrenoceptor agonist, when administered binds beta 2 receptors
   - ✓ Stimulation of adenylate cyclase
   - ✓ Increase cAMP
   - ✓ Bronchodilation and decreased muscular tone

Methylxanthine: Aminophylline, Theophylline

Mechanism of Action

1. Inhibit Phosphodiestrase Enzyme (which catalyzes breakdown of cAMP).
    - ✓ Increase cAMP
    - ✓ Dephosphorylation of MLC
    - ✓ Bronchodilation
2. Increased intracellular calcium
3. Blockade of adenosine receptors: Decrease contractility of bronchiolar smooth muscles

Anticholinergics: Ipratropium, Oxytropiu, Tiotropium

Mechanism of Action

- ✓ Blockade of muscarinic receptors present in bronchi and bronchioles
- ✓ Decrease mucus viscosity
- ✓ Increase mucociliary clearance

Leukotriene Receptor Antagonists

- ✓ Montelukast – oral
- ✓ Zafirlukast – (Cingular) oral administration for control of asthma

Leukotrines are products of arachidonic acid metabolism. They are released at the site of inflammation producing bronchoconstriction having contributory effect to inflammation and bronchoconstriction.

Mechanism of Action

Montelukast and Zafirlukast are competitive antagonists.

- ✓ Inhibits cysteinlyl leukotriene Cys LT1 receptor relieving bronchospasm and bronchoconstriction.
- ✓ Inhibit physiologic actions of LTC4, LTD4, LTE4
- ✓ One drug blocks synthesis of 5 lipo-oxygenase and is hepatotoxic **Zileuton.** Half like is 2.5 hours

Drug Interactions

Zafirleukast has drug interaction with warfarin sodium, leading to increased prothrombin time,thus dose has to be monitored. Monteleukast is commonly used.

Mast Cell Stabilizers

- Na chromoglycate - inhalation
- Nedocromil
- Ketotifen- (5HT action) - oral

Nedocromil and Ketotifen are not bronchodilators, not having direct effect. They are ineffective once antigen antibody reaction takes place.

Mechanism of Action

1. Inhibit transmembrane influx of Ca provoked by antigen antibody interaction on thesurface of mast cells. This is prophylactic use and have to be given before antigen enters.
2. Stabilize mast cells membrane and inhibit release of chemical mediators
3. Depress exaggerated neuronal reflexes triggered by stimulation of irritant receptors
4. Depress axonal reflexes which release inflammatory neuropeptides.
5. Inhibit release of cytokines from T-CELLS

Corticosteroids

- Hydrocortisone **I/V**
- Prednisolone **oral**
- Betamethosone
- Beclomethasone **inhalation**
- Budesonide
- **Flucitasone** having affinity for glucocorticoids receptors in airways

Mechanism of Action

- Anti inflammatory action
- Decrease mucosal oedema, mucus secretion and reduce capillary
- permeabilityStabilize mast cells
- Block immune response, decrease antibody
- formationAntagonise histaminergic and cholinergic responses
- Enhance beta-2 adrenoceptor responsiveness to agonists (Catecholamines)

Ciclesonide

Prodrug, when absorbed drug is acted upon by esterases in bronchial epithelial cells, less amount of drug absorbed gets bound to glucocorticoid receptors, bones, skin, eyes, and there areless chances of osteoporosis and cutaneous thinning.

It has some role in people predisposed to cataract and osteoporosis.

Status Asthmaticus Status asthmaticus is an acute exacerbation of asthma that remains

unresponsive to initial treatment with bronchodilators. It is a life threatening form of asthma, because it can lead to respiratory failure and cardiac arrest. Status Asthmaticus requires immediate treatment (corticosteroids are essential as immediate treatment). Air trapping strains on breathing muscle which are fatigue and exhausted. Status asthmaticus is frequently associated with metabolic acidosis, and acidosis reduces the effectiveness of beta agonist.

1. I/V $NaHCo_3$ added if pH is below 7.5 in patient with refractory status asthmaticus, butthere is risk of hypercapnia, in children.
2. decrease in PCO_2 level corrected with nasal/Face mask oxygen (Helium)
3. Continuous nebulization of albuterol for the first few hrs
4. Switched to intermittent albuterol very 02 hrs. I/V
5. corticosteroids, inhaled ipratropium every 06 hrs

Monoclonal Antibodies: Omalizumab

They bind to IgE antibodies present on mast cells. If administered I/V or subcutaneously, humanized monoclonal antibodies decrease levels of IgE antibodies, decreasing tendency ofsevere asthma, in both phases (immediate/delayed).